



EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion on the substantiation of health claims related to linoleic acid (LA) in combination with gamma-linolenic acid (GLA) and reduction of ocular dryness (ID 4274) pursuant to Article 13(1) of Regulation (EC) No 1924/2006

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SCIENTIFIC OPINION

Scientific Opinion on the substantiation of health claims related to linoleic acid (LA) in combination with gamma-linolenic acid (GLA) and reduction of ocular dryness (ID 4274) pursuant to Article 13(1) of Regulation (EC) No 1924/2006¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2, 3}

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies was asked to provide a scientific opinion on a list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006. This opinion addresses the scientific substantiation of health claims in relation to linoleic acid (LA) in combination with gamma-linolenic acid (GLA) and reduction of ocular dryness. The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The food that is the subject of the health claims is linoleic acid in combination with gamma-linolenic acid. The Panel considers that the food constituents, linoleic acid and gamma-linolenic acid, are sufficiently characterised.

The claimed effect is “ocular comfort”. The target population is assumed to be the general population. In the context of the proposed wordings, the Panel assumes that the claimed effect refers to the reduction of ocular dryness by promoting tear production. The Panel considers that reduction of ocular dryness is a beneficial physiological effect.

No references were provided from which conclusions could be drawn for the scientific substantiation of the claim.

On the basis of the data presented, the Panel concludes that a cause and effect relationship has not been established between the consumption of linoleic acid in combination with gamma-linolenic acid and reduction of ocular dryness.

¹ On request from the European Commission, Question No EFSA-Q-2010-00227, adopted on 13 May 2011.

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KEY WORDS

Linoleic acid, gamma-linolenic acid, n-6 fatty acids, eye, ocular dryness, health claims.

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TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

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EFSA DISCLAIMER

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INFORMATION AS PROVIDED IN THE CONSOLIDATED LIST

The consolidated list of health claims pursuant to Article 13 of Regulation (EC) No 1924/2006⁴ submitted by Member States contains main entry claims with corresponding conditions of use and literature for similar health claims. EFSA has screened all health claims contained in the original consolidated list of Article 13 health claims which was received by EFSA in 2008 using six criteria established by the NDA Panel to identify claims for which EFSA considered sufficient information had been provided for evaluation and those for which more information or clarification was needed before evaluation could be carried out⁵. The clarifications which were received by EFSA through the screening process have been included in the consolidated list. This additional information will serve as clarification to the originally provided information. The information provided in the consolidated list for the health claims which are the subject of this opinion is tabulated in Appendix C.

ASSESSMENT

1. Characterisation of the food/constituent (ID 4274)

The food constituent that is the subject of the health claim is linoleic acid (LA) in combination with gamma-linolenic acid (GLA).

LA (18:2, n-6) is present in various vegetable oils and legumes. In humans, LA is metabolised to GLA and arachidonic acid (ARA), which is further metabolised into eicosanoids of the 2-series. LA can be measured in foods by established methods.

GLA (18:3, n-6) is present in small amounts in a variety of foods of both plant and animal origin, and can also be synthesised in the human body from LA. It is found in relatively high abundance in the plant seed oils of evening primrose, blackcurrant and borage, and in fungal oil (Fan and Chapkin, 1998). GLA can be measured in foods by established methods.

The Panel considers that the food constituents, LA and GLA, which are the subject of the health claim, are sufficiently characterised.

2. Relevance of the claimed effect to human health (ID 4274)

The claimed effect is “ocular comfort”. The Panel assumes that the target population is the general population.

In the context of the proposed wordings, the Panel assumes that the claimed effect refers to the reduction of ocular dryness by promoting tear production.

The Panel considers that reduction of ocular dryness is a beneficial physiological effect.

3. Scientific substantiation of the claimed effect (ID 4274)

One double-blind, randomised, controlled clinical trial investigated the effect of oral n-6 polyunsaturated fatty acids (n-6 PUFAs) (28.5 mg LA and 15 mg GLA twice daily *vs.* placebo) on inflammation markers of the ocular surface (human leukocyte antigen DR (HLA-DR)), measures of

⁴ Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

⁵ EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), 2011. General guidance for stakeholders on the evaluation of Article 13.1, 13.5 and 14 health claims. EFSA Journal, 9(4):2135, 24 pp.

tear production and state of the ocular surface, and ocular dryness symptoms in 26 subjects with keratoconjunctivitis sicca (dry eyes) (Barabino et al., 2003). Patients with and without Sjögren's syndrome were included. Another double-blind, randomised, controlled, clinical trial investigated the effect of oral n-6 PUFAs (112 mg LA and 15 mg GLA twice daily) vs. placebo on prostaglandin E1 (PGE1) tear content, measures of tear production and state of the ocular surface, and ocular dryness symptoms in 40 subjects with Sjögren's syndrome (Aragona et al., 2005). The Panel considers that the evidence provided does not establish that patients with Sjögren's syndrome are representative of the general population with regard to the status of the lacrimal glands, or that results obtained in studies on patients with Sjögren's syndrome can be extrapolated to the general population with regard to ocular dryness.

One double-blind, randomised, clinical trial in 60 subjects investigated the effect of oral n-6 PUFAs (28.5 mg LA and 15.1 mg GLA once daily) vs. no treatment on ocular comfort, measures of tear production, and state of the ocular surface following photorefractive keratectomy (PRK) (Macri et al., 2003). The Panel considers that the evidence provided does not establish that subjects undergoing photorefractive keratectomy are representative of the general population with regard to ocular hydration, or that results obtained in studies on subjects undergoing photorefractive keratectomy can be extrapolated to the general population with regard to ocular dryness.

The Panel notes that no references were provided from which conclusions could be drawn for the scientific substantiation of the claim.

The Panel concludes that a cause and effect relationship has not been established between the consumption of LA in combination with GLA and reduction of ocular dryness.

CONCLUSIONS

On the basis of the data presented, the Panel concludes that:

- The food constituents, LA and GLA, which are the subject of the health claims, are sufficiently characterised.
- The claimed effect is “ocular comfort”. The target population is assumed to be the general population. In the context of the proposed wordings, it is assumed that the claimed effect refers to the reduction of ocular dryness by promoting tear production. Reduction of ocular dryness is a beneficial physiological effect.
- A cause and effect relationship has not been established between the consumption of LA in combination with GLA and reduction of ocular dryness.

DOCUMENTATION PROVIDED TO EFSA

Health claims pursuant to Article 13 of Regulation (EC) No 1924/2006 (No: EFSA-Q-2010-00227). The scientific substantiation is based on the information provided by the Member States in the consolidated list of Article 13 health claims and references that EFSA has received from Member States or directly from stakeholders.

The full list of supporting references as provided to EFSA is available on: <http://www.efsa.europa.eu/panels/nda/claims/article13.htm>.

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- Macri A, Giuffrida S, Amico V, Iester M and Traverso CE, 2003. Effect of linoleic acid and gamma-linolenic acid on tear production, tear clearance and on the ocular surface after photorefractive keratectomy. *Graefe's Archive for Clinical and Experimental Ophthalmology*, 241, 561-566.

APPENDICES

APPENDIX A

BACKGROUND AND TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

The Regulation 1924/2006 on nutrition and health claims made on foods⁶ (hereinafter "the Regulation") entered into force on 19th January 2007.

Article 13 of the Regulation foresees that the Commission shall adopt a Community list of permitted health claims other than those referring to the reduction of disease risk and to children's development and health. This Community list shall be adopted through the Regulatory Committee procedure and following consultation of the European Food Safety Authority (EFSA).

Health claims are defined as "any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health".

In accordance with Article 13 (1) health claims other than those referring to the reduction of disease risk and to children's development and health are health claims describing or referring to:

- a) the role of a nutrient or other substance in growth, development and the functions of the body; or
- b) psychological and behavioural functions; or
- c) without prejudice to Directive 96/8/EC, slimming or weight-control or a reduction in the sense of hunger or an increase in the sense of satiety or to the reduction of the available energy from the diet.

To be included in the Community list of permitted health claims, the claims shall be:

- (i) based on generally accepted scientific evidence; and
- (ii) well understood by the average consumer.

Member States provided the Commission with lists of claims as referred to in Article 13(1) by 31 January 2008 accompanied by the conditions applying to them and by references to the relevant scientific justification. These lists have been consolidated into the list which forms the basis for the EFSA consultation in accordance with Article 13 (3).

ISSUES THAT NEED TO BE CONSIDERED

IMPORTANCE AND PERTINENCE OF THE FOOD⁷

Foods are commonly involved in many different functions⁸ of the body, and for one single food many health claims may therefore be scientifically true. Therefore, the relative importance of food e.g. nutrients in relation to other nutrients for the expressed beneficial effect should be considered: for functions affected by a large number of dietary factors it should be considered whether a reference to a single food is scientifically pertinent.

It should also be considered if the information on the characteristics of the food contains aspects pertinent to the beneficial effect.

⁶ OJ L12, 18/01/2007

⁷ The term 'food' when used in this Terms of Reference refers to a food constituent, the food or the food category.

⁸ The term 'function' when used in this Terms of Reference refers to health claims in Article 13(1)(a), (b) and (c).

SUBSTANTIATION OF CLAIMS BY GENERALLY ACCEPTABLE SCIENTIFIC EVIDENCE

Scientific substantiation is the main aspect to be taken into account to authorise health claims. Claims should be scientifically substantiated by taking into account the totality of the available scientific data, and by weighing the evidence, and shall demonstrate the extent to which:

- (a) the claimed effect of the food is beneficial for human health,
- (b) a cause and effect relationship is established between consumption of the food and the claimed effect in humans (such as: the strength, consistency, specificity, dose-response, and biological plausibility of the relationship),
- (c) the quantity of the food and pattern of consumption required to obtain the claimed effect could reasonably be achieved as part of a balanced diet,
- (d) the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.

EFSA has mentioned in its scientific and technical guidance for the preparation and presentation of the application for authorisation of health claims consistent criteria for the potential sources of scientific data. Such sources may not be available for all health claims. Nevertheless it will be relevant and important that EFSA comments on the availability and quality of such data in order to allow the regulator to judge and make a risk management decision about the acceptability of health claims included in the submitted list.

The scientific evidence about the role of a food on a nutritional or physiological function is not enough to justify the claim. The beneficial effect of the dietary intake has also to be demonstrated. Moreover, the beneficial effect should be significant i.e. satisfactorily demonstrate to beneficially affect identified functions in the body in a way which is relevant to health. Although an appreciation of the beneficial effect in relation to the nutritional status of the European population may be of interest, the presence or absence of the actual need for a nutrient or other substance with nutritional or physiological effect for that population should not, however, condition such considerations.

Different types of effects can be claimed. Claims referring to the maintenance of a function may be distinct from claims referring to the improvement of a function. EFSA may wish to comment whether such different claims comply with the criteria laid down in the Regulation.

WORDING OF HEALTH CLAIMS

Scientific substantiation of health claims is the main aspect on which EFSA's opinion is requested. However, the wording of health claims should also be commented by EFSA in its opinion.

There is potentially a plethora of expressions that may be used to convey the relationship between the food and the function. This may be due to commercial practices, consumer perception and linguistic or cultural differences across the EU. Nevertheless, the wording used to make health claims should be truthful, clear, reliable and useful to the consumer in choosing a healthy diet.

In addition to fulfilling the general principles and conditions of the Regulation laid down in Article 3 and 5, Article 13(1)(a) stipulates that health claims shall describe or refer to "the role of a nutrient or other substance in growth, development and the functions of the body". Therefore, the requirement to describe or refer to the 'role' of a nutrient or substance in growth, development and the functions of the body should be carefully considered.

The specificity of the wording is very important. Health claims such as "Substance X supports the function of the joints" may not sufficiently do so, whereas a claim such as "Substance X helps maintain the flexibility of the joints" would. In the first example of a claim it is unclear which of the various functions of the joints is described or referred to contrary to the latter example which specifies this by using the word "flexibility".

The clarity of the wording is very important. The guiding principle should be that the description or reference to the role of the nutrient or other substance shall be clear and unambiguous and therefore be specified to the extent possible i.e. descriptive words/ terms which can have multiple meanings should be avoided. To this end, wordings like "strengthens your natural defences" or "contain antioxidants" should be considered as well as "may" or "might" as opposed to words like "contributes", "aids" or "helps".

In addition, for functions affected by a large number of dietary factors it should be considered whether wordings such as "indispensable", "necessary", "essential" and "important" reflects the strength of the scientific evidence.

Similar alternative wordings as mentioned above are used for claims relating to different relationships between the various foods and health. It is not the intention of the regulator to adopt a detailed and rigid list of claims where all possible wordings for the different claims are approved. Therefore, it is not required that EFSA comments on each individual wording for each claim unless the wording is strictly pertinent to a specific claim. It would be appreciated though that EFSA may consider and comment generally on such elements relating to wording to ensure the compliance with the criteria laid down in the Regulation.

In doing so the explanation provided for in recital 16 of the Regulation on the notion of the average consumer should be recalled. In addition, such assessment should take into account the particular perspective and/or knowledge in the target group of the claim, if such is indicated or implied.

TERMS OF REFERENCE

HEALTH CLAIMS OTHER THAN THOSE REFERRING TO THE REDUCTION OF DISEASE RISK AND TO CHILDREN'S DEVELOPMENT AND HEALTH

EFSA should in particular consider, and provide advice on the following aspects:

- Whether adequate information is provided on the characteristics of the food pertinent to the beneficial effect.
- Whether the beneficial effect of the food on the function is substantiated by generally accepted scientific evidence by taking into account the totality of the available scientific data, and by weighing the evidence. In this context EFSA is invited to comment on the nature and quality of the totality of the evidence provided according to consistent criteria.
- The specific importance of the food for the claimed effect. For functions affected by a large number of dietary factors whether a reference to a single food is scientifically pertinent.

In addition, EFSA should consider the claimed effect on the function, and provide advice on the extent to which:

- the claimed effect of the food in the identified function is beneficial.
- a cause and effect relationship has been established between consumption of the food and the claimed effect in humans and whether the magnitude of the effect is related to the quantity consumed.
- where appropriate, the effect on the function is significant in relation to the quantity of the food proposed to be consumed and if this quantity could reasonably be consumed as part of a balanced diet.
- the specific study group(s) in which the evidence was obtained is representative of the target population for which the claim is intended.
- the wordings used to express the claimed effect reflect the scientific evidence and complies with the criteria laid down in the Regulation.

When considering these elements EFSA should also provide advice, when appropriate:

- on the appropriate application of Article 10 (2) (c) and (d) in the Regulation, which provides for additional labelling requirements addressed to persons who should avoid using the food; and/or warnings for products that are likely to present a health risk if consumed to excess.

APPENDIX B

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation to the marketing of the food/food constituent, a positive assessment of its safety, nor a decision on whether the food/food constituent is, or is not, classified as foodstuffs. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

It should also be highlighted that the scope, the proposed wordings of the claims and the conditions of use as proposed in the Consolidated List may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 13(3) of Regulation (EC) No 1924/2006.

APPENDIX C

Table 1. Main entry health claims related to is LA in combination with GLA, including conditions of use from similar claims, as proposed in the Consolidated List.

ID	Food or Food constituent	Health Relationship	Proposed wording
4274	The food component is a mix of linoleic acid and gamma-linolenic acid.	Ocular comfort	<p>This fatty acids mix * improves tear quantity</p> <p>This fatty acids mix * contributes to ocular comfort/visual comfort</p> <p>This fatty acids mix * improves lachrymal functions</p> <p>This fatty acids mix * decreases ocular dryness * linoleic acid and gamma-linolenic acid</p>
	<p>Conditions of use</p> <p>- Administration of at least 112 mg of linoleic acid and 15 mg of gamma-linolenic acid twice daily for 45 days.</p>		

GLOSSARY AND ABBREVIATIONS

ARA	Arachidonic acid
GLA	Gamma-linolenic acid
HLA-DR	Human leukocyte antigen DR
LA	Linoleic acid
PGE1	Prostaglandin E1
PRK	Photorefractive keratectomy
PUFA	Polyunsaturated fatty acid